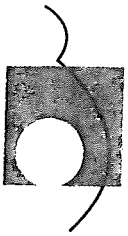
EXHIBIT “B”



THE CENTER FOR WOMEN'S HEALTH CARE

JAMES M WHEELER,MD,MPH,JD

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA, CHARLESTON DIVISION

FRCP Rule 26 EXPERT REPORT OF Dr. James M. Wheeler, MD, MPH, JD

RE: MRS. REBECCA DALBERG [redacted] - PLAINTIFF

My name is Dr. James M. Wheeler, MD, MPH, JD. I am over 18 years of age, and of sound mind, sufficient to author this Expert Report. I have been asked to review the medical records pertaining to Mrs. Dalberg, and determine whether, within a reasonable degree of medical and probability, she suffers complications from the 8/29/2007 implantation of Ethicon polypropylene ("PP") mesh product Prolift™ and Bard PP mesh product Uretex™. All opinions I offer in this Expert Report are made within a reasonable degree of medical and scientific probability applied to the medical records and documents received and reviewed pertaining to care provided to Mrs. Dalberg.

I. Expert's Qualifications

My *curriculum vita* is attached to this Expert Report as Appendix A and is intended to be wholly incorporated into it. Benefiting from a full scholarship, I earned my B.A. from Harvard in 1978, *magna cum laude* in the double major of Biology and Psychology/Social Relations; my research at Harvard resulted in publications describing the anterior hypothalamic control of vertebrate pituitary reproductive function. A full scholarship allowed me to earn a M.D. from Baylor College of Medicine in 1981. From 1981 – 1982, I completed a N.I.H.-funded research fellowship in Medical Endocrinology at Baylor, working within andrology, studying the male side of reproductive function. Also, at Baylor, I completed my residency in Obstetrics & Gynecology ("Ob/Gyn") from 1982 - 1986, serving as Administrative Chief Resident my senior year. During

my medical school and residency training, I took several electives concentrating in urology, including the evaluation, diagnosis, and treatment of women with various maladies the same or similar to those at issue with Mrs. Dalberg. From 1986 – 1988, I completed three post-residency programs at Yale University: 1) a post-residency subspecialty fellowship in Reproductive Endocrinology/Infertility, with half of my clinical time in this program spent in menopausal medicine assigned to thought-leader Dr. Phil Sarrel who taught me many aspects of hormone effects on female urogenital tissues, including the vagina and perivaginal tissues, and resulting effects on sexual function; 2) the Robert Wood Johnson Clinical Scholars program in clinical epidemiology, the science of conducting and interpreting clinical research; and 3) a Master's in Public Health, earning Distinction in the major of Biostatistics and minor of Maternal/Child Health. I later earned my J.D. from the University of Houston Law Center in 2005, concentrating in health law. Most recently, I have completed another credential supporting my review across the breadth of medical topics, a Legal Nurse Consultant ("LNC") certificate. I now teach Legal Research and Medical Law & Ethics to undergraduates, Legal Research and LNC Practices/Principles to nurses at the bachelor's, master's, and doctorate level, and medicolegal consulting to medical students and practicing physicians.

I am board-certified in Ob/Gyn, recertifying annually, most recently in December 2017. I have practiced Ob/Gyn, fulltime and continually since 1986, and have treated thousands of women who had medical issues substantially similar to those Mrs. Dalberg suffered before her implantation surgery. I discuss the relative advantages vs. disadvantages of the various methods of treating urinary incontinence and pelvic organ prolapse, and if surgery is required, I perform preoperative and postoperative evaluation, counseling and treatment. I am clinically competent to evaluate Mrs. Dalberg, and women similarly situated.

I have been a surgical innovator, but only when clinical benefit to my patients was apparent. I was on the early edge of advanced laparoscopic techniques in gynecology, diagnostic and operative hysteroscopy, transvaginal aspiration of oocytes for IVF, and transvaginal ultrasonography. I was the first Ob/Gyn in Houston to perform routine cystoscopy after vaginal hysterectomy to assure bladder and ureter safety. I coauthored a paper on laparoscopic repair of bladder injury at gynecologic surgery. I designed a flexible office hysteroscope for Karl Storz, and contributed to their development of their hysteroscopic pump; I was presented as an expert to

the FDA for hysteroscopic equipment regarding this technology.[1] After co-authoring a paper on occasionally lethal hysteroscopic postoperative hyponatremia,[2] I contributed to the development of an animal model that elucidated the effects of estradiol on a renal ion pump,[3] developed a medical strategy to immediately reduce the risk of hysteroscopic postoperative hyponatremia,[4]and then developed operative hysteroscopic instrumentation that used isotonic uterine distension media[5] – likely preventing deaths from this otherwise minor surgery. Most recently, I developed an abdominal incision with superior surgical exposure and improved cosmesis for women and performed it in several hundred women. As to surgical uses of mesh, I've consulted on the clinical application of abdominal hernia repair with mesh years ago and co-developed a specific type of sacrocolpopexy for vaginal vault prolapse using Goretex patch graft; these results were presented at medical meetings,[6] including Baylor hospitals, and teaching it to our Ob/Gyn residents, regarding the diagnosis and management of mesh-related complications such as infection and erosion.

Throughout my career, I've incorporated advancing clinical practice through careful innovation, but also utilized critical judgment in adopting new technology as it had been presented to me. I have attended many seminars, training sessions, hospital in-services, medical meetings and one-on-one company representative teaching sessions for various new technologies, and yet have exercised what I think to this day was good judgment as to what innovations offered benefit to my patients, and which might not. For example, I always chose to use the first surgical laser taught to me – CO_2 – declining participation using Argon, KTP or YAG lasers as they were presented to me to evaluate by their manufacturers because I failed to see any real advantage for my patients. When asked by Karl Storz, Inc. to join a blue-ribbon panel of Ob/Gyn hysteroscopists to design the 'perfect office hysteroscope', I was the only panel-member of eight who recommended a flexible scope design, yet I was the consultant selected to go forward with this design with the Storz

[1] My travel expenses for this appearance before the FDA was paid by Karl Storz, Inc., but no other payment was made for my participation.
[2] Wheeler CV, Article #23.
[3] Wheeler CV, Article #41, Abstract #54.
[4] Wheeler CV, Article #38, Abstract #51.
[5] I understand I was the first to use Ethicon's/Gynecare's Versapoint hysteroscopic surgical system in the Western hemisphere. That first patient, "V.G.", had a large uterine septum that was at great risk for excessive fluid absorption using prior technology. The Versapoint procedure was uncomplicated, V.G. conceived and delivered a full-term pregnancy, and continues to follow-up in my medical practice doing well.
[6] Wheeler CV, Abstract #45.

engineers. I evaluated new designs of aspiration-guidance sleeves to be attached to ultrasound machines to perform IVF oocyte aspiration, and chose older, simpler, safer designs. I evaluated various types of ultrasound probes for use in surgery and declined to participate in research and clinical use for new probes that I believe lacked benefit. I evaluated ultrasound-guided radiofrequency uterine fibroid ablation and chose myomectomy as the best method by which to manage clinically symptomatic fibroids. Similarly, I rejected the advances proposed to me regarding uterine artery embolization for fibroid treatment. I declined to develop new surgical instruments at laparotomy, for cost containment, as the instruments I used worked adequately. When asked to evaluate the da Vinci surgical robot, I felt it not to be cost effective, preferring the assistance of my surgical nurse on even complicated gynecologic surgery. Regarding membrane research, I've done animal research using amnion to prevent postoperative adhesions; my introduction to mesh research was via another material to prevent postoperative adhesions – serving as an early clinical and clinical research advisor on Ethicon's TC-7 Interceed™ mesh product. I've evaluated and published with a leader in vaginal surgery in Houston, our combined case series on sacrocolpopexy using Goretex patch graft. As to polypropylene vaginal mesh, I attended many presentations and training sessions of the PP vaginal mesh products as each was introduced to the practitioners at the hospital at which I practiced. None of the PP mesh products represented superior prospects to my patients with stress urinary incontinence or pelvic organ prolapse. Instead, I chose to continue with a modified open Burch colposuspension in SUI patients and sacrocolpopexy in POP patients, with minimal complications, rare recurrence/reoperation, and predictable improvement of symptoms. Very specifically to my evaluation of the mesh for vaginal implantation, I had, and continue to have, these concerns for their use in my patients: 1) a vaginal approach and resulting introduction of bacterial contamination in the presence of a foreign body; 2) the blind use of trocars in anatomically variable spaces (when the mesh had to be applied with a trocar); 3) increased possibility of bladder and blood vessel complications compared to Burch procedures; 4) the effects of placing large pieces of foreign material – as compared to a few sutures and native tissues – in the very sensitive peri-urethral and peri-vaginal areas; 5) the physical properties of the various meshes over time; and 6) the predictable effect the meshes – either without complication, but especially with complications of infection or erosion – would have on patients' sexual function.

Although I chose to never implant polypropylene ("PP") mesh products into the peri-vaginal area for the reasons outlined above, I have taken care of many dozens of women who have been implanted with a wide range of PP mesh products available to treat SUI and POP. Not unexpectedly, I have provided care to dozens of women with the range of complications known to be due to PP mesh, including erosion/extrusion, recurrent SUI and POP, reoperation for these indications, various pain syndromes including dyspareunia, abnormal bleeding, urinary tract infections, and unusual immunologic-mediated syndromes, such as suburethral granuloma to systemic autoimmune like syndrome. I attest that I am sufficiently experienced at PP mesh complications to offer the opinions within this report.

In forming my opinions, I utilize both my clinical experience and knowledge outlined above, as well as my knowledge of the methodology by which that clinical experience is studied and presented to fellow practitioners. I am an experienced laboratory and clinical scientist, having published dozens of peer-reviewed journal articles, book chapters, and abstracts, all of which are listed in my CV. My publications reflect my concentration in methodology across the clinical fields in which I have interest. As the first surgical specialist accepted into Yale's Robert Wood Johnson Clinical Scholars Program, I sought to promote improved methodologic rigor in Ob/Gyn clinical research. As such, I introduced concepts of pelvic mapping to improve recordation of surgical findings.[7] I helped conduct Phase III[8] and Phase IV[9] clinical trials on medications used in Ob/Gyn. I published an improved study design and statistical analysis in fertility studies, including the introduction of Kaplan-Meier life table analysis.[10] I published on various biases, and their management, in clinical research, e.g. selection bias, and detection and minimizing the effects of confounding.[11] I published on innovative concepts in clinical practice, including combining medical and surgical treatments, vs. medical *or* surgical,[12] endometriosis as a bimodal (i.e. mild vs. severe) disease rather than a linear disease (mild, moderate to severe) disease, and minimal endometriosis as a normal anatomic variant rather than true 'disease'.[13] I designed and helped lead education programs to Ob/Gyn professional societies (e.g. American Association of Gynecologic

[7] Wheeler CV, Article #28, Abstracts #7, 20, 34.
[8] Wheeler CV, Articles #22,24 and Abstracts #7, 48, 49.
[9] Wheeler CV, Articles #31, 32, 33, 34.
[10] Wheeler CV, Articles #13, 16, 21, 28, 29, 36 and Abstracts # 33, 37.
[11] Wheeler CV, Article #29, and Abstracts #21, 25, 30, 31, 32, 33 39, and 46.
[12] Wheeler CV, Articles #2, 15 and Abstracts #8, 10, 13 and 23.
[13] Wheeler CV, Articles #13, 21, 28.

Laparoscopists ("AAGL") and the American College of Obstetricians and Gynecologists (ACOG) regarding improving study designs and statistical analysis for Ob/Gyn researchers.

I have undertaken several steps to improve my knowledge of biomaterials. I have participated in bench research involving endocrinology and reproduction. I have worked with biologic membranes and synthetic membranes to prevent postoperative adhesions. I have worked with biomaterials in the various innovations outlined above over the course of my career. Most recently I have completed an intensive course on biomaterials intended for bioengineers, including pelvic meshes; that course leader has also supervised me in a directed reading as to the biomateriality of pelvic meshes.[14]

I have experience in the policy aspects of litigation such as Mrs. Dalberg's. As a national officer of ACOG, I served several years on their Health Care Commission, writing and co-editing a variety of pieces on health policy affecting all Ob/Gyns in the U.S. and their patients. Part of my M.P.H. program and Clinical Scholars Program at Yale involved the evaluation, generation, and improvement of health care policy involving topics including Maternal/Child Health, but also topics beyond. In law school, I studied the legal aspects of policy development through the law. And as a trained mediator and arbitrator, I've studied methods by which policy disagreements can be satisfactorily negotiated.

Based upon the myriad of my education, training, research, experience, and knowledge, I present myself to the Court as a uniquely trained and experienced clinician, researcher, and methodologist, and as such, am suitably and sufficiently qualified to explain the clinical course of Mrs. Dalberg, and to explain how her vaginal PP mesh procedures directly caused her complications, leading to her current clinical situation.

II. Expert's Methodology of Testimony

Within my understanding of my role in Mrs. Dalberg's case, it is my specific intent to be helpful to the finders of fact, recognizing that I myself do not serve in that role. I intend to base my

[14] It was an honor at this University of Washington course led by Dr. Buddy Ratner to have my research on the innovative drug delivery system used in Depo-Lupron cited, and my introduction to the class from the audience.

opinions on a reliable foundation of medical record review, expert testimony review, and medical literature review – which are all standard methods by which a medical expert gives his own expert opinion, and considered generally reliable, and certainly frequently relied upon in litigation. I intend my testimony to relate to specific issues within Mrs. Dalberg's case; I intend to be helpful in the assessment of her case, while maintaining some efficiency of communication with the reader in terms of the length and breadth of this Report.

I will be incorporating methodologic tools of a clinical epidemiologist, namely medical literature review and synthesis, in the expression of my opinions herein. Such methodologic tools are standard, accepted and often incorporated into the opinions expressed by many experts – but are simply not spoken as predicated upon a foundation within clinical epidemiology, with biostatistics support. I will also, as a testifying clinician, be incorporating the specific clinical and scientific methodology dealing with "Differential Diagnosis". "Differential diagnosis" is a standard scientific technique of listing the most likely causes of a medical problem, then eliminate less likely causes based on the facts of the case and scientific knowledge, finally ending up with the most probable cause by deductive reasoning and logic. I intend my differential diagnosis to be of appropriate breadth, incorporating any reasonably likely candidates causing a particular medical issue; however, possible causes of an infinitesimal degree would not be included. For example, applicable to Mrs. Dalberg's case, differential diagnosis appropriately applied to her symptom of recurrent cystocele would include Prolift™ PP mesh failure, *de novo* POP, increasing trauma including new employment or exercise causing increased intrabdominal pressure, and other less likely causes. Applying differential diagnosis to pelvic pain, appropriately reasonable possible causes include interstitial cystitis, endometriosis and diverticulitis which can be clinically suspected by history and physical examination, but must be confirmed by specific medical procedures, namely, cystoscopy, laparoscopy, and colonoscopy/CT scan, respectively.

I may be opining as to some aspects of Mrs. Dalberg's emotions and thinking as reasonably derived from her records. My background for this role is having graduated with departmental *summa cum laude* honors in the co-major of Psychology/Social Relations from Harvard, but more relevant, from the training and experience in this aspect of patient care from 35+ years of medical training and practice. I will respect my limitations of clinical assessment of emotions and mentation; for example, I recognize I do not possess particular insight into the *mens* of a corporate

entity, or without privileged information, the members of a particular corporate entity. And I recognize the limitations of any review based on record review, vs. being a treating physician.

III. Pertinent Clinical History re: Mrs. Rebecca Dalberg

I have reviewed these documents in arriving to my opinions expressed in this report:

- Hospital records from Scott & White Metroplex Health System;
- Records from Dr. Mark Lobaugh, M.D.;
- Records from Dr. Bernard Morris, M.D.;
- Records from Dr. Charles Mitchell, M.D.;
- Records from Scott & White Temple Clinic/Dr. Erin Bird, M.D.; and
- Plaintiff Fact Sheet.

Mrs. Dalberg is now 69 years of age; she was 58 at time of her PP mesh implantations on 8/29/2007. She has had four vaginal deliveries in 1967, 1968, 1969, and 1970; she is married to Mr. Cornelius Dalberg.[15] At the time of her mesh products implantation in August 2007, Mrs. Dalberg was diagnosed with significant medical co-morbidities of atherosclerotic heart disease, systemic lupus erythematosus, hypertension, gastroesophageal reflux disease, and anxiety; she did not have diabetes.[16] She had a limited smoking history, reporting smoking in 2001-2002.[17] The medical records reviewed date back to 2005; in July 2005, Mrs. Dalberg had undergone laparoscopic cholecystectomy complicated by perforation of the transverse colon, which upon emergent exploration on 7/29/2005, "dime-sized area of the proximal transverse colon" covered with "extremely dense fibrosis" represented a perforation that "had apparently sealed on its own", sufficiently effective enough that bowel contents were not found in the abdominal cavity.[18] She also had undergone prior hysterectomy, appendectomy, tonsillectomy, and arthroscopic knee surgery; she had previously had a concussion with some cognitive sequela.[19]

In 2007, Dr. Mark Lobaugh diagnosed Mrs. Dalberg with SUI with low urethral pressure, and POP characterized by cystocele, rectocele, and vaginal vault prolapse. On 8/29/2007, he

[15] Plaintiff Fact Sheet, p 3, p 12.
[16] Metroplex records, p 492.
[17] Plaintiff Fact Sheet, p 20.
[18] Metroplex records, pp 153-154.
[19] Ibid., p 493, p 492.

performed extracorporeal colporrhaphy, anterior colporrhaphy, posterior colporrhaphy, enterocele repair, perineoplasty and urethropexy; Ethicon/Gynecare's Prolift™ PP mesh augmented the colporrhaphies and Bard's Uretex™ was used for the "transvaginal tape urethropexy".[20] Cystoscopy after implantations was without bladder perforation, and no complications were recorded. On Postop Day #1, Mrs. Dalberg had some transient chest pain throughout the evening after surgery, with no relief obtained with a sublingual nitroglycerin tablet given.[21] Mrs. Dalberg is recorded to have attributed this pain to "her anxiety disorder"; the consultant agreed to follow her through her hospitalization and as an outpatient.[22]

A note is made of Mrs. Dalberg having a retrograde cystourethrogram on 5/23/2008, but without other details noted.[23] In late 2009, Mrs. Dalberg presented with a history of "recurrent voiding symptoms including urgency, frequency, and pelvic pain", as well as nausea, vomiting, and recurrent urinary tract infections; record is made "her symptoms began after a bladder prolapse repair" with mesh; physical exam demonstrated "diffuse tenderness of the anterior pelvic wall and irregularities consistent with possible erosion of the cystocele/artificial mesh material".[24] Vaginoscopy and cystoscopy on 12/18/2009 diagnosed "infected, eroded artificial sling material".[25] The oral antibiotic Keflex was prescribed following this diagnostic procedure.[26]

On 1/5/2010, Mrs. Dalberg underwent exploration and excision of "infected eroded vaginal sling"[27]; the erosion was "easily seen predominantly on the right side at the level of the bladder base". "Dense inflammatory responsive scar tissue" surrounded the sling mesh. The majority of the sling material was excised, but the wings extending up toward the retropubic space could not be easily excised was left in place.[28] Final pathology of removal of the "infected vaginal sling" demonstrated "polarizable foreign material, foreign body giant cell inflammation and fibrosis

[20] Ibid., pp 506-508. Prolift, "PFRT01" lot no. 3020684 was implanted (p 3).
[21] Ibid., p 492.
[22] Ibid, p 492, p 494.
[23] Ibid., p 382, "Procedure History".
[24] Ibid., p 358, by Dr. Charles Mitchell.
[25] Ibid., pp 7-8, by Dr. Bernard Morris.
[26] Ibid., p 359.
[27] Ibid., p 353.
[28] Ibid., p 369, by Dr. Bernard D. Morris.

consistent with excised vagina sling and associated with inflammation and fibrosis (clinically infected vaginal sling".[29] Mrs. Dalberg was discharged home on 1/6/2010, to be seen in a week.[30]

On 1/27/2010, Dr. Morris saw Mrs. Dalberg, recording she has "a small residual tail of the mesh on each side of the pelvis that could not be safely accessed from below" at his surgery.[31] On 3/31/2010, Dr. Morris notes Mrs. Dalberg is "voiding without complaints" and is feeling "much better", but "still has occasional pains particularly in the left pelvic area"; there was no tenderness noted vaginally.[32]

On 5/6/2010, for persistent pain, Dr. Morris made an incision from umbilicus to pubis, and suprapubically removed "infected mesh from anterior repair and pubovaginal sling", complicated by an incidental cystotomy necessary for removal of the mesh.[33] Progress note on 5/10/2010 noting "status post removal of infected mesh from the anterior repair",[34] "patient had a fever of 103 degrees", with concern of "intrabdominal infection or sepsis"; multiple antibiotics were prescribed intravenously.[35] CT scan on 5/11/2010 identified "complex fluid collection above and slightly anterior to the symphysis pubis", with differential diagnosis including abscess vs. mild herniated bladder.[36] "Postoperative cellulitis" was diagnosed on 5/12/2010,[37] and on 5/14/2010, Dr. Morris explored the pelvis and repaired an incisional hernia, using nylon retention sutures with bridges.[38] Mrs. Dalberg was noted to be improving the next day, on 5/17/2010.[39] Mrs. Dalberg was discharged to outpatient follow-up on 5/18/201.[40] Follow-up on 6/6/2011 "after extensive pelvic surgery to remove infected foreign body" noted "her original pain is gone", with "mild irritative voiding symptoms and no leakage" present.[41]

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[29] Ibid., pp 384-385, by Dr. Phillip Day.
[30] Ibid., p 353.
[31] Ibid., p 9.
[32] Ibid., p 11.
[33] Ibid., p 2.
[34] Ibid., p 1062, by Dr. Hemalkumar Ramani.
[35] Ibid.
[36] Ibid., p 1042.
[37] Ibid., p 1060.
[38] Ibid., p 1011.
[39] Ibid., p 1056.
[40] Ibid., p 986.
[41] Ibid., p 13.

On 9/20/2010, noting "return of urinary leakage" of mixed type, with the SUI "significantly more bothersome" refractory to a trial of anticholinergic medical therapy, Dr. Morris recommended urodynamics be performed.[42] Cystography on 10/19/2010 demonstrated anterior/inferior impression on the bladder related to prior cystocele repair, mild post void residual, and otherwise normal findings[43] Dr. Erin Bird concluded "it appears the patient has a devastated urethra with severe type 3 urinary incontinence.[44]

On 12/1/2010, Dr. Morris noted a bulge in the area of the left abdominal incision where the abdominal mesh removal had been performed. On 12/29/10, Dr. Gail Burbridge repaired the "4 cm in diameter" "direct hernia through the floor of the inguinal canal", incorporating a "2 X 4-inch polypropylene mesh prosthesis"[45] and Dr. Morris injected Contigen for coaptation of proximal urethral tissue.[46] Follow-up on 6/13/2011 noted Mrs. Dalberg to be "on maximal medical management with Ditropan and Vesicare", and having urinary incontinence and severe bladder instability.[47]

Notation is made on 6/27/2011 of "incontinence occurring constantly", caused by "coughing, laughing, and sneezing", with insensible and urge components as well.[48] Note on 12/12/2011 states Mrs. Dalberg "was leaking again" with a brown color.[49] On 2/7/2012, noting Type 1 SUI and grade 1-2 cystourethrocele,[50] Dr. Morris performed "a needleless sling" at the level of the mid-urethra.[51]

On 9/23/2014, Dr. Bird noted Mrs. Dalberg underwent "injections for incontinence a total of five times, most recently in March 2014 and August 2014", with initial improvement than going back to incontinence. Mrs. Dalberg reported constant leaking of urine, using 6-10 pads a day, voiding

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[42] Ibid., p 16.
[43] Ibid., p 172.
[44] Ibid., pp 156-157.
[45] Ibid., p 861.
[46] Ibid., p 861, p 862. A total of "3 syringes of Coaptite were used".
[47] Ibid., p 20.
[48] Ibid., p 164.
[49] Ibid., p 21.
[50] Ibid., p 747.
[51] Ibid., p 758.

every two hours, nocturia thrice nightly, and feeling like "she always has to go".[52] Options were discussed, and surgery was consented.

On 12/11/2014, Dr. Bird performed autologous fascial sling placement and repair of vesicovaginal fistula.[53] Transurethral catheter was removed on 12/15, with suprapubic tube remaining;[54] suprapubic tube was working well on 12/26/2014[55] and 12/29/2014.[56] On 1/26/2015, Dr. Bird pronounced Mrs. Dalberg had a "devastated urethra that will likely not be amenable to urethral continence and normal voiding"; Mrs. Dalberg was "understandably upset by this."[57]

On 3/26/2015, cystometrics demonstrated "gravitational urinary incontinence due to a devastated urethra."[58] Cystoscopy the same day "again noted mesh erosion of posterior vagina", with findings of a gaping bladder neck, constant leakage through the urethra, and no leakage into the vagina when the urethra was temporarily obstructed.[59] Note is made of "attempted urethral closure for 'devastated urethra' after mesh complications" on 4/16/2015, with suprapubic tube change-out on 7/13/2015;[60] recordation of suprapubic tube leaking "with painful spasms" was also made.[61]

On 11/12/2015, Dr. Bird performed cystoscopy, diagnosing a "5 French vesicovaginal fistula and non-pliable vaginal tissue".[62] On11/19/2015, Dr. Bird performed cystoscopy and periurethral bulking therapy using Coaptite as an attempt to close off the vesicovaginal fistula; "good coaptation was achieved" using 3 ml of Coaptite.[63]

On 12/30/2015, Dr. Bird again operated on Mrs. Dalberg, repairing vesicovaginal fistula with a successful closure noted.[64] At postop follow-up on 3/8/2016, Mrs. Dalberg "had been dry until 5 days prior" to the visit, noting continuous leakage of urine.[65] Dr. Bird concluded "I made sure

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[52] Ibid., p 47.
[53] Ibid., p 82.
[54] Ibid.
[55] Ibid., p 84.
[56] Ibid., p 94.
[57] Ibid., p 105.
[58] Ibid., p 116.
[59] Ibid., p 119.
[60] Ibid., p 146.
[61] Ibid.
[62] Ibid., p 41
[63] Ibid., p 32.
[64] Ibid., p 37.
[65] Ibid., p 38.

they understood that I do not believe she has any more good options" due to "her tissues being very unfavorable".[66]

IV. Prior Expert Testimony Reviewed re: Polypropylene ("PP") Mesh

I have been provided these documents, listed chronologically by date submitted, which I have reviewed to help provide context in reviewing Mrs. Dalberg's case:

- Expert Report of Dr. Michael Thomas Margolis, dated 10/14/2013;
- Expert Reports of Dr. Peggy Pence, PhD, dated 10/14/2013, 7/17/2014, and 3/2/2016;
- Expert reports of Dr. Expert Report of Dr. Bruce Rosenzweig, dated 1/22/2016;
- Expert Report of Dr. Daniel Elliott, dated 1/25/2016;
- Expert Report of Dr. Scott Guelcher, dated 1/25/2016;
- Expert Report of Dr. Bob Shull, dated 2/1/2016;
- Expert Report of Dr. Vladimir Iakovlev, dated 2/1/2016;
- Expert Report of Dr. Jerry G. Blaivas, dated 2/1/2016;
- Expert Report of Dr. Brian J. Flynn, dated 2/26/2016;
- Expert Report of Shelly F. Thames, dated 3/1/2016;
- Expert Report of Dr. John Miklos (undated);
- Expert Report of Dr. Alan D. Garely (undated);
- Expert Report of Ms. Anne Wilson, MBA (undated); and
- Expert Report of Mr. Timothy A. Ulatowski, M.S (undated).

Having reviewed these Experts' testimony in litigation involving vaginal uses of PP mesh,[67] various opinions from this expanse of very learned experts are of relevance to Mrs. Dalberg's case. Recognizing the voluminous nature of the opinions, exhibits, and supporting literature of the many Experts in this litigation, *in toto,* I will excerpt opinions particularly relevant to Mrs. Dalberg's case from each expert's written report, in the chronologic order in which their submission was dated, after parsing the experts into "Clinicians" who see and treat patients like

[66] Ibid., p 39.

[67] There is some generalizability of these Experts' opinions, whether addressing Prosima, Gynemesh, Prolift, or TVT products including TVT/TVT-O/TVT-Secur – any of Ethicon's polypropylene meshes for use for SUI or POP.

Mrs. Dalberg, or analyze tissue from such patients, such as pathologists, and "Non-Clinicians" with additional areas of expertise other than provision of clinical care, all of whom are pertinent to Mrs. Dalberg's case.

IV.A. CLINICIAN OPINIONS REGARDING POLYPROPYLENE ("PP") MESH

Dr. Michael Thomas Margolis, M.D., dated 10/14/2013:

Dr. Margolis is an extremely well trained urogynecologist, culminating in being a member of the first class of Board-Certified Pelvic Surgeons in the U.S.[68] He has ample experience in surgical management of prior gynecologic surgery, including "prolapse, incontinence, fistulas, and polypropylene or other synthetic mesh and sling related injuries."[69] Dr. Margolis opines that "TVT", by which he seems to represent the span of PP mesh products,[70] can cause a list of complications, some of which are represented within Mrs. Dalberg's case including mesh erosion and degradation of mesh could necessitate future surgery.[71]

Dr. Bruce Rosenzweig, M.D., dated 1/22/2016:

Another well trained urogynecologist, Dr. Rosenzweig has performed over a thousand pelvic floor procedures.[72] Additionally, for a clinician, he has a particular focus on the physical properties of PP mesh; he opines as to the pore size and fibrotic bridging of PP mesh,[73] as well as the concerns about the hydrogen peroxide and microbes found in the vagina potentially aggravating PP mesh placement to the point of producing chronic inflammation.[74] Dr. Rosenzweig's report, and his opinions expressed within, were supported by cited medical literature regarding these aspects of polypropylene mesh:

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[68] Dr. Margolis Report, p 2.
[69] Ibid., p 3. Note that complications occur in the presence, but also the absence, of mesh products, interpreting the words of this sentence in Dr. Margolis' Report.
[70] See FN 26 above re: the generalizability between all forms of Ethicon's PP mesh products based on the use of PP mesh within each of them.
[71] Ibid., pp 5-6.
[72] Dr. Rosenzweig's Report, pp 1-2.
[73] Ibid., p 30.
[74] Ibid., pp 16, 17, 23. These factors, among others including laser cut of the mesh (p13) and mesh degradation (pp 13, 17) contributed to Dr. Rosenzweig's opinion that "Prolene mesh is not suitable" for its use in vaginal repairs (p 12).

- High overall complication rates using polypropylene mesh: Clave' A et al. (2010);[75]
- The vagina as a source of hydrogen peroxide to degrade PP mesh: Strus M et al. (2006);[76]
- Micro-organisms can contribute to PP mesh degradation: Das N & Chandran P (2011);[77]
- Degradation of PP via oxidation "begins in just a few days" in an animal model;[78]
- "[A] lot of PP shrink to about 30-50% of their original size" in animal studies;[79]
- Of the "more than 200" meshes available, certain physical characteristics of the mesh, including pore size, affects inflammation and fibrosis: Klinge U et al. (2013);[80]
- TVT mesh erosion indicating reoperation has been known for years: Kuuva N (2006);[81] and
- Various products, but not all, have been preceded by thorough research: Nilsson C (2015).[82]

Dr. Daniel Elliott, M.D., dated 1/25/2016:

Dr. Elliott is a Mayo Clinic Urology professor, specializing in the treatment of POP and SUI for 15+ years, and published in an animal model studying PP mesh.[83] Dr. Elliott testified that PP mesh causes inflammation and does indeed degrade,[84] and shrinks and contracts, and should not be used

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[75] Dr. Rosenzweig's reference no. 21: Clave' A, Yahi H, Hammou JC, Montanari S, Gounon P, Clave' H: Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. "This study provides evidence contrary to published literature characterizing polypropylene as inert" in pelvic floor reinforcement applications. These authors suggested that polyester prosthetics ('polyethylene terephthalate – PET) may be more inert *in vivo.*"

[76] Dr. Rosenzweig's ref. no. 23: Strus M, Brzychczy-Wloch, Gosiewski T, Kochan P, Heczko P: The in vitro effect of hydrogen peroxide on vaginal microbial communities. FEMS Immunol Med Microbiol 2006. 48:56-63. "...hydrogen peroxide produced by lactobacilli plays a pivotal role in controlling vaginal flora", p 62.

[77] Dr. Rosenzweig's ref. no 25: Das N & Chandran P: Microbial degradation of petroleum hydrocarbon contaminants: an overview. Biotechnology Research International, 2011, Article ID 941810.

[78] Dr. Rosenzweig's ref. 26: Liebert TC, Chartoff RP, Cosgrove SL, McCuskey RS: Subcutaneous implants of polypropylene filaments. J Biomed Mater Res. 1976 Nov; 10(6):939-951.

[79] Dr. Rosenzweig's ref. 41a: Klinge U, Klosterhalfen B, Juller M, Ottinger AP, Schumpelick V: Shrinking of polypropylene mesh in vivo: an experimental study in dogs. Eur J Surg. 1998 Dec;164(12):965-969.

[80] Dr. Rosenzweig's ref. 41: Klinge U, Park J-K, Klosterhalfen B: 'The Ideal Mesh?' Pathobiology 2013. 80:169-175. "Sufficiently large pores as well as structural stability in case of mechanical strain have been identified to be crucial to reduce excessive inflammation and fibrosis. Furthermore, large pores prevent bridging of the foreign body reaction through the pore and thereby help to reduce clinical adverse events as erosion, shrinkage, or pain." (p 169).

[81] Dr. Rosenzweig's ref. 136: Kuuva N, Nilsson CG: Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women. Acta Obstet Gynecol Scand. 2006;85(4):482-487. "The tape was visualized in 3.1% of the women and necessitated resection in 1.6%...", Abstract.

[82] Dr. Rosenzweig's refs. 145, 146: Nilsson CG: Creating a gold standard surgical procedure: the development and implementation of TVT. Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015. 26:787-789. "Some launches have been preceded by thorough clinical documentation and others not". (p 787). "Recent history includes the launch and withdrawal of many modifications and copies of the TVT procedure, which shows that any variation of a procedure needs its own thorough clinical testing before it can be accepted for common use." (p 789).

[83] Dr. Elliott's Report, p 1.

[84] Ibid., pp 20, 13.

in the presence of peroxides.[85] He testifies as to the cytotoxicity of PP mesh, and the risk of scarring and foreign body reactions.[86] Dr. Elliott opines about some physical aspects of PP mesh including laser cutting, and concludes his report discussing numerous clinical concerns including faulty insertion techniques and poor training of surgeons.[87]

Dr. Bob Shull, M.D., dated 2/1/2016:

Dr. Shull is a senior gynecologist very highly regarded for his work in pelvic floor disorders of women, including SUI and POP. In his report, after a modest introduction of his background, Dr. Shull explains:

> "[T]he characteristics of PP mesh when implanted vaginally for POP include chronic inflammation, foreign body reaction, fibrosis and scarring, nerve entrapment, deformation, stiffening, shrinkage and contraction, and degradation have clinical significance."[88]

Dr. Shull details these consequences of vaginally implanting heavyweight, small pore PP mesh as causing foreseeable complications later in his report, citing supportive medical literature.[89]

Dr. Shull summarizes his opinions in the body of his Expert Report regarding Ethicon's vaginal mesh products, including:

1) Ethicon failed to inform physicians as to which patients were poor candidates for PP mesh;
2) After reviewing the Prolift™ medical literature, specifically, Dr. Shull opines:

-Ethicon did not perform proper clinical trials to demonstrate the safety and efficacy of its PP mesh devices; and

-The literature does not support using PP mesh for treatment of pelvic organ prolapse.[90]

Dr. Jerry G. Blaivas, M.D., dated 2/1/2016:

Dr. Blaivas is a senior urologist who pioneered sling surgery for incontinent women. He is well published, including the 2015 review article, "Safety considerations for synthetic sling surgery" in Nature Reviews Urology.[91] Dr. Blavias testifies that PP mesh "should not have been designed for

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[85] Ibid., pp 24, 18.
[86] Ibid., pp 27, 24.
[87] Ibid., p 30, 34, 43.
[88] Dr. Shull's report, p 2.
[89] Ibid., p 6.
[90] Ibid., pp 15-29.
[91] Dr. Blaivas' Report, p 3. "The Nature family of journals is regarded as one, if not *the* premier resource for scientific research in the world."

placement in a surgically contaminated field without proper animal and clinical studies to document safety, and without a clear warning about the possibility of short- and long-term complications."[92] He opines about the physical characteristics of PP mesh, including pore size and laser cutting,[93] and degradation as reported by pathologist Dr. Iakovlev et al.[94] Dr. Blaivas cites ample medical literature supporting his opinions, of relevance in evaluating Mrs. Dalberg's case, including:

- Avoiding mesh use in areas of the body with "any level of contamination": Choi JJ (2012);[95]
- The long-term nature of physical and emotional mesh complications: Dunn GE (2014);[96]
- Persistence of symptoms following removal of PP mesh: Hammett J et al. (2014);[97]
- Recurrence of SUI after sling excision surgery: Blaivas JG, et al. (2015);[98] and,
- Underreporting of major complications of midurethral slings: Deng DY et al. (2007).[99]

Dr. Brian J. Flynn, M.D., dated 2/26/2016:

Dr. Flynn is a well-trained and experienced urologist, who has done hundreds of operations for SUI using PP mesh, especially the TVT line of products. Of note, after reviewing the history of SUI surgery, and stating his preference for TVT products, he does not actually exclude Burch

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[92] Ibid., p 4.
[93] Ibid., pp 16-17.
[94] Ibid., p 18. Dr. Iakovlev's opinions are discussed *infra*.
[95] Dr. Blaivas ref. 7: Choi JJ, Palaniappa NC, Dallas KB, Rudich TB, Colon MJ, Divino CM: Use of mesh during ventral hernia repair in clean-contaminated and contaminated cases: outcomes of 33,832 cases. Ann Surg 2012. Jan;255(1):176-180. "There is a significant increase in risk of postoperative occurrences following ventral hernia repairs using mesh in clean-contaminated and contaminated cases relative to clean cases. We recommend avoiding the use of mesh in any level of contamination." (Abstract).
[96] Dr. Blaivas ref. 9: Dunn GE, Hansen BL, Egger MJ, Nygaard I, Sanchez-Birkhead AC, Hsu Y, Clark L: Changed women: the long-term impact of vaginal mesh complications. Years after mesh placement, including physical and emotional pain, caused "cascading health problems", "a spiral of health problems, anxiety and desperation". Abstract.
[97] Dr. Blaivas ref. 9: Hammett J, Peters A, Trowbridge E, Hullfish K: Short-term surgical outcomes and characteristics of patients with mesh complications from pelvic organ prolapse and stress urinary incontinence surgery. Int Urogynecol J 2014. Apr;25(4):465-470. After mesh excision by experienced pelvic surgeons "a significant number of patients may have persistent symptoms following surgery". Abstract.
[98] Dr. Blaivas ref 11, which is his 'Nature' article: Blaivas JG, Purohit RS, Benedon MS, Mekel G, Stern M, Billah M, Olugbade K, Bendavid R, Iakovlev V: Safety considerations for synthetic sling surgery. Nat Rev Urol 2015. Sep;12(9):481-509. Dr. Blaivas et al. states an "additional risk" includes "refractory overactive bladder, fistulas and bowel perforations", and the "overall risk of a negative outcome after synthetic midurethral sling implantation surgery is $\geq$ 15%." Abstract.
[99] Dr. Blaivas ref 12, 49: Deng DY, Rutman M, Raz S, Rodriguez LV: Presentation and management of major complications of midurethral slings: are complications under-reported? Neurourol Urodyn 2007;26(1):46-52. Abstract.

colposuspensions as a viable alternative[100] for those women whose POP is associated with SUI symptomatology.

Dr. John Miklos, M.D. (undated):

Dr. Miklos is well-trained with fellowships in Urogynecology and Laparoscopic surgery and is very published in the use of synthetic or allogenic grafts and gained valuable European experience with PP mesh use. Dr. Miklos testifies to the complications of the PP mesh product as including "Recurrence of SUI incontinence."[101]

Dr. Alan D. Garely, M.D. (undated)

Dr. Garely is a fellowship-trained Urogynecologist, with training in PP mesh going back to 1998 when he trained on Gynecare TVT at the Karolinska Institute in Sweden. Dr. Garely once served in a consultative role with Ethicon regarding their mesh products.[102] Dr. Garely's opinions more general opinions are related to Ethicon's Prolift™ product, but much of this report focuses upon a modification of Prolift™, called "Prolift + M.™"

Dr. Vladimir Iakovlev, dated 2/1/2016:

Dr. Iakovlev is an anatomic pathologist who has done extensive research on explanted PP meshes;[103] however, he did not perform clinical pathologist clinical care on the women from whom the mesh specimens were removed. He testified as to PP degradation, and mesh migration.[104] His summary opinion was:

> "The (polypropylene) mesh acts as a foreign object and the body attempts to degrade and isolate the mesh. The mesh itself, as a foreign object, and the body reaction to the mesh damage the tissues in a critical anatomical location. This damage occurs in all patients, however, to a variable degree between the patients. The manifestations range from subclinical to fully developed complications triggering mesh excision."[105]

Dr. Iakovlev then systematically describes each of the elements of his summary opinion.[106] The PP mesh is implanted in a "critical anatomical location", the perivaginal spaces, causing "foreign

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[100] Dr. Flynn's report, p 10. Later, Dr. Flynn states the Burch and Paravaginal Suspension should be reserved for "risk factors" for mesh operations, or "failed TVT" (p 19).
[101] Dr. Miklos' report, pp 24-25.
[102] Dr. Alan D. Garely's report, p 23.
[103] Dr. Iakovlev report, p 5.
[104] Ibid., pp 8 and 12, respectively.
[105] Ibid, p 14.
[106] Ibid., pp 14-20.

body inflammation", which induces "scar ingrowth and encapsulation". This scar causes "mesh contraction", and due to impact on "mesh-scar innervation", "involvement of neural ganglia", and the high nerve density of the "innervation of female genital organs", various types of pain result. The mesh-scar plate becomes "stiff" and "irregular", tender and painful, causing "tissue edema" due to the inflammatory chemical mediators. "Skeletal muscle" and "smooth muscle" tissues can be involved and affect the sensation and function of pelvic organs like the bladder, vagina and rectum. "Vascular (damage via) thrombosis and obliteration" parallels neural damage. Degrading mesh can "fold and curl", and "migrate" partly due to the inflammatory response pushing the mesh-scar complex. "Mucosal erosion of the mesh is a complication for the mesh surgeries; it cannot happen without the use of mesh". The two mechanisms for erosion are migration and breakdown of the overlying mucosa; erosion causes "acute inflammation". "Polypropylene degradation" is gradual over "years in the body", and "cracking of degraded" PP mesh is seen "immediately after mesh is removed" from the body. It is just such findings in explanted tissues upon which Dr. Iakovlev presents his findings, concluding there is "correlation with internal Ethicon documents".

IV.B. NON-CLINICIAN EXPERT OPINIONS RE: POLYPROPYLENE ("PP") MESH

Dr. Peggy Pence, PhD, dated 10/14/2013, 7/17/2014, and 3/2/2016:

Dr. Pence is a scientist with an impressive >40 years' experience in pharmaceuticals, biopharmaceuticals, and medical devices, having worked for Eli Lilly, Serono, and Berlex.[107] In her 2013 report, Dr. Pence outlines the development of the PP line of mesh implants, beginning with the suture material Prolene™ in 1976, then the development of PP mesh products into the 1990's and early 2000's.[108] She then details a variety of concerns with the biocompatibility of PP mesh within women, including host responses, shrinkage/contracture, degradation, fraying, deformation, cytotoxicity, and carcinogenicity.[109] Dr. Pence opines that "Ethicon knew early" of PP mesh's risks for complications,[110] and she criticizes Ethicon for its "failure to conduct appropriate testing" of PP meshes including its line of TVTs.[111] Dr. Pence expresses additional opinions that Ethicon failed to warn physicians about TVT's risks, that TVT was misbranded and

[107] Dr. Pence, 2013, p 1.
[108] Ibid., pp 34-41.
[109] Ibid., p 41, p 45, p 46, p 50 p 51.
[110] Ibid., p 49.
[111] Ibid., p 53, et seq.

mislabeled, and Ethicon failed to conduct adequate post-marketing vigilance of its TVT products.[112]

In Dr. Pence's 2014 Expert Report,[113] reviews her opinions about various aspects of biocompatibility of PP mesh as not being inert to host response, was prone to shrinkage/contracture, degradation, fraying/roping/deformation, cytotoxicity and potential carcinogenicity based on one case report.[114] Dr. Pence in 2014 opined that Ethicon erred in its management of its line of PP mesh products by failing to conduct sufficient testing, misleading practitioners, and misleading products.[115]

Dr. Pence's 2016 Supplement followed the production of ample discovery within this litigation, giving her cause to further develop her opinions, but "not change any of my opinions as a result of my review of these additional materials."[116] Dr. Pence cited that "experts concluded that prospective studies should be performed … including exhaustive documentation of adverse events"[117] of PP mesh implants into women.

Dr. Scott Guelcher, dated 1/25/2016:

Dr. Guelcher is a Ph.D. Chemical Engineer, with laudatory training and experience in biomedical products. Complimentary to the same-minded clinicians, including his co-author anatomic pathologist Dr. Iakovlev,[118] Dr. Guelcher opined that PP reacts with molecular oxygen in the body, resulting in embrittling the mesh, causing a foreign body reaction for an indefinite period – unless the PP is removed in its entirety. That is, PP mesh is not inert and its properties change after implantation, "which can lead to adverse events in an implantee",[119] such as Mrs. Dalberg.

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[112] Ibid., p 72, p 84, p 89, p 108.
[113] Dr. Pence's Expert Report of 7/17/2014, p 42.
[114] Ibid., p 43, p 44, pp 45-47, p 53, p, 54-57.
[115] Ibid., p 58, pp 69-70, p 103.
[116] Dr. Pences' 2016 Supplement, p 1.
[117] Ibid., p 3.
[118] Dr. Guelcher report, ref. no. 88: Iakovlev VV, Guelcher SA, Bendavid R. In vivo degradation of polypropylene: microscopic analysis of meshes explanted from 130 patients. J Biomed Mater Biomater 2015, Aug 28. Abstract.
[119] Dr. Guelcher report, p 18. Regarding Ethicon's research, Dr. Guelcher summarizes: "Ethicon scientists reported evidence of chronic inflammation, oxidation and degradation (micro-cracking of Prolene in preclinical studies and in human explants..." "Despite the fact that Ethicon scientists recommended additional testing to confirm or exclude the oxidation mechanism, I have found no evidence that these tests (which were available to Ethicon during development of the SUI and POP devices) were performed. Consequently, the risks inherent to Prolene™

Ms. Anne Holland Wilson, MBA:

Ms. Wilson is a Biomedical Engineer and Quality Assurance Consultant.[120] After reviewing some Ethicon procedures, Ms. Wilson focuses on the mesh's physical properties: "polypropylene's susceptibility to in vivo degradation",[121] and the "increased stiffness of laser cut mesh".[122] The latter third of her report reviews aspects of physician technique and learning curves thereof, and Ethicon's Instructions for Use and updating procedures.[123]

Mr. Timothy A. Ulatowski, M.S.:

Mr. Ulatowski is an expert in FDA procedures and labelling. He testifies that he found no problems with Ethicon's brochures, labeling procedures, or interactions with the FDA.[124]

V. Relevant Medical Literature Review

Because I am a physician with formal training in clinical epidemiology, bolstered by a Master's degree in biostatistics, I routinely review the medical literature relevant to any individual's case I'm asked to review. Then, looking at the quantity and quality of the research, I am able to draw upon my formal training in methodology and opine conclusions – including those involving causation. Specifically, my clinical epidemiology and statistics training help me make very reliable and cogent arguments as to causation; several examples will serve to better explain my abilities in methodology. I am an expert in biases and faulty study designs that may masquerade or hide causation. I am expert in not over-concluding causation, such as when a possible cause and effect are simply related temporally. I am expert in confounding variables – a factor that has a relationship to a purported cause, and a purported effect, but does not actually mean the cause is directly linked to the effect. I am especially trained in conducting a review of the medical literature, and gleaning relevant aspects towards a particular case, like Mrs. Dalberg's. Very broadly, historically, the scope of the problem of stress urinary incontinence ("SUI") and pelvic

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oxidation and degradation are *detrimental to all of those who have been implanted* with the SUI and POP devices." (p 19). (Emphasis added).

[120] Ms. Wilson report, p 1.

[121] Ibid., pp 16-17.

[122] Ibid., pp 17-18.

[123] Ibid., pp 18-22.

[124] Mr. Ulatowski report, p 50.

organ prolapse ("POP") within the general population is immense. It is estimated that up to 50% of women in the U.S. have urinary incontinence, with 80% of those having at least an element of SUI.[125] Colposuspensions, typically of the Burch type with many modifications, and mid-urethral slings were shown to be effective within the literature for in SUI.[126] Mrs. Dalberg was implanted with the Ethicon PP mesh product Prolift™ augmenting her anterior vaginal repair and the Bard PP mesh product Uretex™ for SUI on 8/29/2007. A review of the clinical literature can provide valuable information on a suspected cause-effect relationship between the Prolift™ and Uretex™ PP mesh products and Mrs. Dalberg's exceedingly complicated post-implantation course. Results from a MEDLINE search will be first presented regarding Prolift™, followed by one for Uretex.™

V. A. MEDICAL LITERATURE RE: ETHICON/GYNECARE'S PP MESH, PROLIFT™

Using a MEDLINE search engine like PubMed, this is quite straightforward, procedurally. The search term "Prolift" produced over 140 citations; when cross-referenced with "complications", 80-plus citations were produced and all were screened for relevance to Mrs. Dalberg's case in particular; several citations are selected for particular relevance to Mrs. Dalberg's symptoms and signs and are presented below.

The Prolift™ polypropylene mesh system to treat anterior or posterior, or combined anterior/posterior, compartment genital prolapse was introduced in 2005; it was withdrawn from the market in early 2013 due to safety concerns.[127] It was initially thought to merge the benefits of apical vaginal suspension as in sacrocolpopexy with those of transvaginal plication techniques, using a low-weight (42.7 g/m^2), thin (0.42 mm) and high-porosity (64%) one-thread preformed polypropylene prosthesis synthetic graft.[128]

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[125] Nambiar A, Cody JD, Jefferey ST: Single-incision sling operations for urinary incontinence in women (Review). The Cochrane Collaborative. 2014. John Wiley & Sons, Ltd., p 2.
[126] Ibid.
[127] Kozal S, Ribert T, Bayoud Y, Menard J, Nicolacopoulos I, Bednarzych L, Staerman F, Larre' S: Morbidity and functional mid-term outcomes using Prolift pelvic floor repair systems. Can Urol Assoc J 2014;8(9-10).
[128] Ibid., p E605.

Concern with a "higher inflammatory response…likely due to polypropylene mesh" was raised in abdominal hernioplasties well before Prolift was introduced in 2005.[129] In gynecology, concern was expressed that "the vagina is a clean-contaminated environment, and it is not possible to insert polypropylene ("PP") mesh devices without bacterial contamination…"[130] Greater surface areas of PP mesh would increase inflammatory response, fibrous stimulation, and erosion; degradation of PP would lead to potentially greater inflammation. Scar tissue contracted the PP mesh to less than 50% of its implanted size, causing pelvic pain, and erosion into adjacent organs via migration. This same author, Dr. Donald R. Ostergard, in 2011 wrote a summary of the Food & Drug Administration ("FDA") activities of various meshes and mesh kits, including PP mesh;[131] Dr. Ostergard concludes his timeline with this entry: "2010 – Degradation occurs in all currently used meshes",[132] and concludes his article with, "Many publications detailed degradation mechanisms including heat exposure during manufacture and bacterial colonization of the polypropylene used in pelvic repair meshes".[133] More recent articles also focus on the features of PP degradation including inflammation, cracking, and increased brittleness using light microscopy[134] and electron microscopy.[135]

Wetta et al. (2009) also described complications following Prolift PP mesh placement: groin pain, and UTI's, both considered minor complications.[136] Mrs. Dalberg developed pelvic pain concomitant with her mesh erosion diagnosis.

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[129] Di Vita G, Milan S, Frazzetta M, Patti R, Palazzolo V, Barbera C, Ferlazzo V, Leo P, Ciliari E: Tension-free hernia repair is associated with an increase in inflammatory response markers against the mesh. Am J Surg 2000 Sep;180(3):203-207.

[130] Ostergard DR: Obstet Gynecol 2010 Oct;116(4):962-966. *See also, from 2012 Journal of Urology,* Sternschuss G, Ostergard DR, Patel H: Post-implantation alterations to polypropylene in the human. J Urol 2012 Jul;188(1):27-32. Abstract.

[131] Ostergard DR: Degradation, infection and heat effects on polypropylene mesh for pelvic implantation: what was known and when it was known. Int Urogynecol J 2011. 22:771-774. This review notes in bold the original FDA clearance of ProteGen Sling Mesh Kit on Nov 15, 1996, and the FDA clearance letter of TVT on Jan 28, 1998. Prolene Soft Mesh™ was FDA cleared May 23, 2000.

[132] Ibid., p 773, citing Clave A, Yahi H, Hammou J-C, Montanari S, Gounon P, Clave H: Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. Internat Urogyn J 2010. 21:261-270.

[133] Ibid., p 773.

[134] Iakovlev VV, Guelcher SA, Bendavid R: Degradation of polypropylene in vivo: A microscopic analysis of meshes explanted from patients. J Biomed Mater Res B Appl Biomater 2015 Aug 25. Abstract.

[135] Imel A, Malmgren T, Dadmun M, Gido S, Mays J: In vivo oxidative degradation of polypropylene pelvic mesh. Biomaterials 2015. Dec;73:131-141. Abstract.

[136] Ibid., p 4.

A study of 524 patients treated with Prolift™ PP mesh reported a reoperation rate, such as Mrs. Dalberg experienced, was 11.6%.[137] Longer-term complications, like reoperation, PP mesh erosion, and recurrent POP with or without varying degrees of SUI often takes longer follow-up for clinicians to recognize.

A PubMed search on Prolift™ papers over the last few years demonstrates additional findings about Prolift™ after its U.S. market withdrawal in 2013. Although currently off the market, "many women underwent Prolift™ mesh augmentation, and long-term postoperative outcome assessments are relevant and important."[138] These U.S. authors did follow-up in women with anterior, posterior and combination Prolift™ procedures, and found dyspareunia in 36% with 4.3% requiring surgical revision. Vaginal tenderness was noted in 45% of patients, with vaginal stricture in 2.1%; Mrs. Dalberg experienced both vaginal tenderness along the mesh edges, and contracture of the mesh necessitating surgical release. Mesh exposure was seen in 6.4%, all of whom had discontinued estrogen therapy postoperatively and had significant vaginal atrophy noted.[139] Contemporaneous international reports of Prolift™ erosion included incidence of mesh erosion in 3.1%[140] and 8%[141] of patients; a contemporaneous U.S. study demonstrated mesh exposure confirmed in 12.6% of Prolift™ implantees, sometimes associated with postoperative back pain.[142] Comparison studies demonstrated Prolift™ to be at greater risk for mesh exposure than other PP

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[137] de Landsheere L, Ismail S, Lucot JP, Deken V, Foidart JM, Cosson M: Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study included 524 patients with 3 years' median follow-up. Am J Obstet Gynecol 2012 Jan;206(1):83, e1-7. Abstract.

[138] Meyer I, McGwin G, Swain TA, Alvarez MD, Ellington DR, Richter HE: Synthetic graft augmentation in vaginal prolapse surgery: Long-term objective and subjective outcomes. J Minim Invasive Gynecol 2016; 23(4):614-621.

[139] Ibid., p 618.

[140] Song W, Kim TH, Chung JW, Cho WJ, Lee HN, Lee YS, Lee KS: Anatomical and functional outcomes of Prolift transvaginal mesh for treatment of pelvic organ prolapse. Low Urin Tract Symptoms 2016 Sep;8(3):159-164. Abstract. These patients were treated with partial excision of the mesh with no evidence of infection.

[141] Li BH, Huang HJ, Song YF: Modified Prolift procedure without trachelectomy or hysterectomy for the treatment of advanced pelvic organ prolapse complicated with cervical elongation. Zhonghua Fu Chan Ke Za Zhi, 2016 Mar;51(3):174-179. Abstract. The 6 mesh exposures occurred at 3-9 months after Prolift implantation.

[142] Illston J, Garris J, Richter H, Wheeler T II: Pain scores and exposure rates after polypropylene mesh for pelvic organ prolapse. South Med J 2015 Dec;108(12):715-721, p 718. This 12.6% exposure rate was conservative; for all known erosion cases (10 out of 45 examined patients), the erosion rate calculated to 22.2%. Graft exposure was associated with postoperative back pain and hematoma formation (p 718).

mesh products,[143] specifically when compared to American Medical System's Elevate™.[144] Recent articles also identified Prolift™ as posing a greater risk of persistent SUI,[145] and higher incidence of POP manifested by vaginal bulge symptoms.[146]

V. B. MEDICAL LITERATURE RE: BARD'S PP MESH, URETEX™

A Pubmed-search of MEDLINE using the search term "Uretex" produced ten citations, several of which were in non-English language journals. It is similar to Gynecare's original retropubic TVT device; it can be placed infrapubically or suprapubically, depending on surgeon's experience and choice.[147] Uretex is a polypropylene monofilament microporous sling and a steel needle introducer with a blue guide tube; the specific design "ensures no 'sling' effect and no particle release while maintaining elasticity and high porosity for an optimized tissue ingrowth".[148] This cited French study of 53 patients had a mesh erosion rate by 1 year of follow-up of 3.5%, and a bladder perforation rate of 10.5%.[149]

A study with 3-year follow-up of 75 patients implanted with Uretex™ reported "medium-term" morbidity of de novo urgency (5%), urinary frequency (4%), and urge incontinence in 1%; no graft erosions were noted.[150] In comparison studies to Ethicon/Gynecare's retropubic TVT™ sling,

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[143] Wu PY, Chang CH, Shen MR, Chou CY, Yang YC, Huang YF: Seeking new surgical predictors of mesh exposure after transvaginal mesh repair. Int Urogynecol J 2016 Oct;27(10);1547-1555. Abstract. Prolift™ mesh significantly increased the risk of erosion 5-fold (HR 5.52, 95% CI 1.15-26.53, p = 0.033)

[144] Rogowski A, Bienkowski P, Tarwacki D, Szafarowska M, Samochowiec J, Sienkiewicz-Jarosz H, Jerzak M, Baranowski W: Retrospective comparison between the Prolift™ and Elevate™ anterior vaginal mesh procedures: 18-month clinical outcome. Int Urogynecol J 2015 Dec;26(12):1815-1820. Abstract. The mesh erosion proportion of 7.7% for Prolift was significantly higher than that of Elevate (0%; p = 0.02).

[145] Lo TS, Nawawi EA, Wu PY, bt Karim N, Al-Kharabsheh A: Predictors for persistent urodynamic stress incontinence following extensive pelvic reconstructive surgery with and without midurethral sling. Int Urogynecol J 2016 Mar;27(3):399-406. Abstract. In patients with concomitant SUI surgery with Prolift, the risk of persistent SUI was 3-fold greater than other products (OR 3.1, 95% CI 1.9-4; p < 0.001).

[146] Barros-Pereira I, Valentim-Lourenco A, Fonseca A, Melo B, Henriques A, Ribeirinho A: A retrospective analysis of the effectiveness of anterior pelvic organ prolapse repair with Prolift™ versus Elevate™ vaginal mesh. Int J Gynaecol Obstet 2017 Nov;139(2):192-196. Abstract. Prolift patients had 18% incidence of bulge symptoms at 12 months' follow-up vs. 7% in the Elevate group (p = 0.021).

[147] Cortesse A, Jacquetin B, Grise P, Le Normand L, Richard F, Haab F: Prospective multicenter clinical trial of Uretex Sup for surgical treatment of SUI. Internation J Urol 2007. 14:611-615, p 611.

[148] Ibid., p 612, p 615. The authors state the blue needle guide also makes bladder perforation especially easy to identify cystoscopically.

[149] Ibid., p 613.

[150] Gebhart JB, Dixon DA, Trabuco EC, Klingele CJ, Bagniewski SM, Weaver AL: Three-year outcomes of Uretex Urethral Support System for treatment of SUI. Int Urogynecol J Pelvic Floor Dysfunct 2008 Aug;19(8):1075-1079. Abstract.

comparative research demonstrated Uretex™ and TVT had similar short-term improvements in SUI and complications observed.[151]

VI. Experts' Reports & Medical Literature Applied to Mrs. Dalberg's Case

This review of the Prior Expert Testimony[152] and review of the Relevant Medical Literature[153] cited above, allows this clinician/methodologist to conclude that the most probable cause of Mrs. Dalberg's symptoms and signs is the physical characteristics of the polypropylene mesh itself that was implanted into Mrs. Dalberg as Ethicon/Gynecare's PP mesh product Prolift™ and Bard's PP mesh product Uretex™ in August 2007. The physical characteristics of the PP mesh that directly caused Mrs. Dalberg's complications include: 1) the use of a stiffer heavyweight weave of PP, vs. a more pliable lighter or medium weave; 2) small pore size vs. larger pore size that causes fibrotic bridging instead of ingrowth of healthy healing tissue; and 3) laser cut vs. mechanical cut which contributes to the fragmentation and degradation of the polypropylene. These physical characteristics of the PP mesh, in the Experts' Opinions reviewed and the Medical Literature cited, combine to cause a foreign body reaction and cytotoxicity, inducing chronic inflammation, oxidation and degradation of the PP mesh. The degradation of the PP mesh then directly and proximately causes a myriad of clinically-appreciated complications, including shrinkage and deformation of the implant causing pain, foreign body reaction and inflammation causing pain and tenderness, PP oxidation and particle release culminating in product failure manifested by recurrent SUI and/or POP. The variability of this degradation process is explained by the characteristics of the PP mesh within the specific product implanted, and the specific characteristics of the host herself. A more robust, more immediate inflammatory response cause vaginal erosion and pain syndromes; more gradual, chronic inflammation leads to slower product degradation and gradual product failure culminating in long-term recurrent SUI or POP, chronic pain syndromes, and chronic infection and inflammatory conditions. Although the exact clinical presentation of each patient will vary according to her own host characteristics, it is the physical

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[151] Novi JM, Mulvihill BH: Surgical intervention for SUI: comparison of midurethral sling procedures. J Am Osteopath Assoc 2008 Nov;108(11):634-638. Abstract.

[152] Citing the expert reports of Drs. Margolis, Rosenzweig, Elliott, Shull, Blaivas, Iakovlev, Guelcher, and Ms. Wilson, abstracted above.

[153] Citing Ostergard (2010) and Ostergard (2011) above.

properties of each of the PP meshes that comprises the underlying biological foundation of each of the patient's clinical symptoms and signs.

One of the factors affecting mesh complications, in terms of incidence but also specific presentation of complication, is "surgical mesh load". Just as mesh weight is an important characteristic of the mesh material itself, with lighter-weight mesh less associated with many in situ complications, various mesh products have strived to reduce the "surgical mesh load" by supplying smaller mesh surface areas.

The findings from having reviewed both Prior Experts' Reports and Relevant Medical Literature regarding complications of polypropylene mesh, including Prolift™, can be applied to Mrs. Dalberg's symptoms and signs following her Prolift™ placement and complications. Having weighed the strength of association between PP mesh and Mrs. Dalberg's findings based on the information found within the Experts' Reports and Relevant Medical Literature, I will conclude my Report by presenting her findings as those that are medically probable, due to the implanted PP mesh Prolift™ in the anterior vaginal wall and PP mesh Uretex™ suburethrally in 2007:

1). *Mesh infection, erosion, and multiple reoperations*

On 8/29/2007, Mrs. Dalberg underwent Uretex™ transvaginal urethropexy and Prolift™ augmented anterior colporrhaphy for SUI and POP. In late 2009, Mrs. Dalberg developed urinary urgency and frequency, pelvic pain, and recurrent urinary tract infections; pelvic exam demonstrated diffusely tender anterior vaginal wall. Vaginoscopy on 12/18/2009 diagnosed "infected eroded vaginal sling; partial resection of the sling was performed 1/5/2010. Due to persistent pain in May 2010, Mrs. Dalberg underwent suprapubic removal of infected mesh from the sling ***and*** the anterior repair; this operation was complicated by infection requiring a CT scan, and reoperation with incisional hernia repair on 5/14/2010. Thereafter, Mrs. Dalberg underwent another sling operation in 2011, multiple periurethral injections with Coaptite, attempts at correcting vesicovaginal fistulae in 2014 and 2015, and finally a failed procedure to close off the urethra and rely upon suprapubic drainage. Dr. Dalberg's physicians declare her urethra as "devastated" with "no good options left".

Mesh infection and erosion are the most mesh-specific complications possible; but for the implantation of the mesh, it could not be infected or erode. Differential diagnosis for these severe

complications is modest in Mrs. Dalberg; although she did have lupus and arteriosclerosis, she was not diabetic, seemingly immunosuppressed, or a clinically significant smoker. There is no history of additional vaginal trauma. In reasonable medical probability, I conclude that it was the mesh products that caused infection and erosion, necessitating numerous subsequent operations and procedures. More specifically, it was the large pore and heavyweight nature of the PP mesh in the products implanted that directly and proximately caused Mrs. Dalberg's infections, erosions, and reoperations. If alternative techniques including sacrocolpopexy and Burch colposuspension, or alternative materials such as biologic grafts, or even PP mesh with larger pore size and lighter weight had been used, it is probable that Mrs. Dalberg would not have experienced this devastating series of reoperations and complications.

2). *Recurrent incontinence*

Dr. Lobaugh performed the original PP mesh implants for SUI, accompanied by POP, in 2007. Voiding symptoms mostly of an urge type occurred in 2009. In 2011, incontinence as characterized as "constant", caused by "coughing, laughing, and sneezing" typical of SUI; she also had an urge component to her incontinence as well. With two episodes of vesicovaginal fistulae, Mrs. Dalberg ultimately suffered truly constant incontinence, and no final correction was deemed possible.

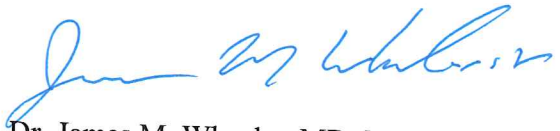
The implantation of the PP mesh did resolve Mrs. Dalberg's original SUI, but then a much more complicated incontinence picture resulted. The recurrent incontinence was intertwined with the infection and erosion of the mesh implants but turned Mrs. Dalberg into a urologic cripple. Differential diagnosis would include other bladder diseases, neuromuscular disease, or rarer syndromes; in Mrs. Dalberg's course, the causative link is clearly traced to the implantation of PP mesh. Specifically, in medical probability, it is the small pore size and heavy weight of the PP meshes implanted into Mrs. Dalberg that caused the recurrent incontinence with which she continues to suffer. If alternative techniques or materials had been used, it is medically probable that these complications would have been prevented. Further, if larger pore lighter weight PP mesh had been used, the complicated recurrent urinary incontinence could have been prevented.

I have reviewed Mrs. Dalberg's medical records, Expert Reports of many qualified experts, and have searched the relevant medical literature pertaining to Ethicon's PP mesh product, Prolift™, and Bard's PP mesh product, Uretex™, which were implanted into Mrs. Dalberg. Her story is notable for the startling number of operations and treatments her complications necessitated following mesh implantation – and she will continue to be at risk for more operations, as indicated in these records. Based on the totality of this information, I am able to attest that it is clearly proven that implanting PP mesh into the human vagina causes foreign body reaction, inflammation, and degradation sufficient to cause a myriad of clinical symptoms and signs including pain, tenderness, infection, mesh erosion, failure of vaginal repair, recurrent SUI, recurrent POP, and reoperation. I have understanding of what clinicians seek before recommending a treatment to their patients, and no reasonable physician would want to implant a known cause of foreign body reaction and inflammation into sensitive vaginal tissues. No reasonable physician, if he or she were warned of the foreseeable consequences of implanting PP mesh, with its physical characteristics of heavy-weight, small pore-size, and laser cut edges causing degradation in the vaginal environment, would conclude the potential benefit of implanting PP mesh into their patients would supersede the risks of implantation. With suitable alternative materials, and alternative procedures, available to the patient with SUI or POP, no reasonable physician would subject his or her patient to the dangers, potentially for the rest of her life, of an implant as faulty as Ethicon's PP mesh product Prolift™.

I appreciate the opportunity to have reviewed Mrs. Dalberg's case. I would appreciate the opportunity to review any information obtained through discovery that could affect my opinions, and if warranted, the opportunity to append my opinions with an addendum. If I may be of further assistance, please contact me.

Respectfully submitted,

April 19, 2018



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